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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,708	12/20/2001	Michael R. Boyd	213045	9974

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EXAMINER	
MITCHELL, GREGORY W	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,708	BOYD, MICHAEL R.	
	Examiner	Art Unit	
	Gregory W. Mitchell	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *18-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

This Office Action is in response to the Remarks and Amendments filed March 03, 2005. Claims 1-2, 5-6, 8 and 31 have been amended. Claims 18-30 are withdrawn from consideration. Claims 1-17 and 31 are examined herein.

Applicant's amendments have necessitated the withdrawal of the rejections and objections of the Office Action dated November 30, 2004. The following rejections now apply.

Election/Restrictions

In the Examiner Interview conducted on February 22, 2005, Applicant requested examination of and Examiner agreed to examine method claims wherein the Z linker would be limited to 7-10 atoms (to form a lactone between 12 and 15 atoms long). Claims 18-30 remain withdrawn from consideration as lacking a common special technical feature with the method claims of the method claims for the reasons of record and furthermore, as amended, the composition claims share no common technical feature with the elected method claims because there are no compounds that meet the composition claims of 18-30 that also meet the elected invention.

Claim Objections

Claim 1 is objected to because of the following informalities: there is a comma immediately following "thereof" and preceding the period at the end of the sentence. Appropriate correction is required.

Claims 6-11 are objected to as containing non-elected subject matter. Notably, claims 6 and 7 encompass compounds wherein the lactone is less than 12 atoms long (i.e. wherein Z, if present, would be less than 7 atoms long).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 12-17 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd et al. (WO 99/05136) in view of Oku et al. (WO 99/21835) and Simon et al. (2002/0042079).

Boyd et al. discloses a method of treating cancer by administering a pharmaceutical composition comprising a compound of formula (I) found therein (Abstract). The treatment of solid tumor cancers, particularly tumors of the lung, brain, kidney and breast and melanomas are disclosed (p. 10). Boyd et al. specifically discloses salicylihalamide A and salicylihalamide B as compounds useful in the method disclosed therein (p. 9). The effective amount of the compounds are disclosed to be that which provides an effective blood level of from 10^{-11}-10^{-7} M (p. 13). Boyd et al. does not specifically teach the administration of the apicularen A or B nor does it specifically disclose the treatment of intra-organellar acidification of intracellular organelles.

Oku et al. teaches malignant tumors (e.g. those related to melanoma and lung cancers) are known to be treatable by vacuolar type H+-ATPase inhibition (pp. 15-16).

Simon et al., it is known in the art that the enhanced sensitivity of tumor cells to chemotherapeutics is a consequence of a reduced acidification within the organelles ([0187]).

It would have been obvious, absent a showing of unexpected results, to one of ordinary skill in the art at the time of the invention to administer a composition of apicularen A or B because such compounds are within the scope of the compounds taught by Boyd et al. to be useful. Accordingly the skilled artisan would have been motivated to utilize apicularen A or B in a treatment of Boyd et al. because of an expectation of similar success in treating the cancers disclosed therein.

It is noted that while other pathways are possible for the treatment of cancers, such as lung tumors, the administration of the compounds of Boyd et al. would obviously meet the claims because Oku et al. teaches that it is known in the art to treat cancers by inhibiting vacuolar type H+-ATPase and Simon et al. teaches that it is known in the art to enhance the treatment of cancer by reducing acidification within the organelles. Accordingly, the treatment of, e.g., a lung tumor of Boyd et al. would meet the conditions of "A method of treating an intra-organellar acidification of intracellular organelles by the inhibition of vacular-type (H+)-ATPase" because a claim for the administration of the same compound to the same population is not rendered patentable by the discovery of a new mechanism by which the treatment works.

Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd et al., Oku et al. and Simon et al. as applied to claims 6-7 above, and further in view of Holt et al. (WO 93/18652) and Yamamoto et al. (*Cell Struct. Funct.* 1998, **23**, 33-42)

Boyd et al., Oku et al. and Simon et al. apply as disclosed above. Boyd et al. further teaches a treatment of cancer comprising the administration of an additional anticancer agent (p. 11), but does not specifically teach an additional component to be administered in the treatment of cancer selected from the group consisting of bafilomycins and concanamycins.

Holt et al. teaches the administration of bafilomycins (ATPase inhibitors) for the inhibition of cancers (Abstract, p. 2).

Yamamoto et al. teaches that the V-ATPase inhibition activity of bafilomycin A_1 is related to its cause of autophagy in rat hepatoma cell lines (cancer) (Abstract; pp. 33-34 and 40). Yamamoto et al. also teaches the equivalence of the V-ATPase inhibition activities of bafilomycin A_1 and concanamycins (pp. 40-41).

It would have been obvious to one of ordinary skill in the art to substitute the additional anticancer agent of Boyd et al. with a bafilomycin of Holt et al. because, as taught by Holt et al., bafilomycins are known to be administered for the inhibition of cancer. One would have been motivated to substitute the generic anticancer agent of Boyd et al. with a bafilomycin because of an expectation of success in treating cancer, as taught by Boyd et al. Furthermore, it would have been obvious to specifically use bafilomycin A_1 as the bafilomycin or to substitute the bafilomycin with concanamycin A

in the treatment rendered obvious by Boyd et al. and Yamamoto et al. because (1) bafilomycin A1 is a bafilomycin; (2) bafilomycin A_1 is taught by Yamamoto et al. to cause atophagy in cancer cells; (3) concamamycins are taught to be the functional equivalent of bafilomycin A_1 by Yamamoto et al.; and (4) concamamycin A is a concamamycin.

Response to Arguments

Applicant argues that because "a given vacuolar-type (H+)-inhibitory compound may preferentially inhibit vacuolar-type (H+)-ATPase activity in one or more kind or location of intracellular organelle, plasma membrane, cell or tissue" the inherent feature of Boyd et al. is not inevitable. Accordingly, Applicant argues, Boyd et al. is not anticipatory of the instant claims. This argument is not persuasive because the prior art teaches the administration of the same compounds as instantly claimed. The administration of the same compound in the prior art will have the same effect as discovered by an applicant whether or not that effect was disclosed by the applicant. A product and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). Futhermore, because Simon et al. teaches that it is known in the art that the treatment of tumor cells is known to be associated with a reduction acidification within the organelles, the treatment of tumors will, inherently, meet the instant claims.

Applicant's arguments that Holt et al. and/or Yamamoto et al. do not remedy the deficiencies of Boyd et al. are not persuasive because it is Examiner's position that the treatment of, e.g., lung tumors with the compounds of Boyd et al. will, inherently, meet the claims, given the teachings of Oku et al. and Simon et al.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER